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Periorbital pigmented skin tags and milia

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A 4-year-old girl presented for evaluation of an increasing number of pigmented lesions on the face and trunk that first started to appear at age 6 months. Her medical history was remarkable for congenital macrocephaly for which a cranial MRI at age 9 months showed no abnormalities. She was otherwise healthy with age-appropriate development. Family history was unremarkable. Physical examination revealed Fitzpatrick phototype III skin and multiple periorbital dark brown and black soft papules of 3-5 mm size along with multiple milia (Figure 1). Similar pigmented lesions were found on the upper trunk and abdomen (Figure 2). Dermoscopy findings are presented in Figure 3. Furthermore, she exhibited a high forehead with frontal bossing. A shave biopsy of one of the pigmented papules on the neck was performed (Figure 4).

FIGURE 1

FIGURE 2

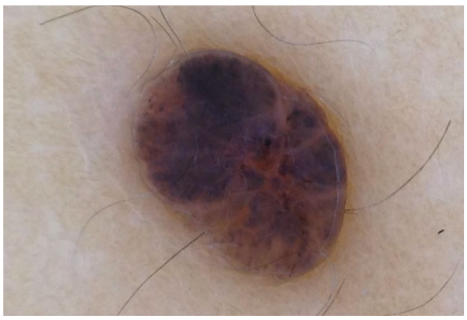

FIGURE 3

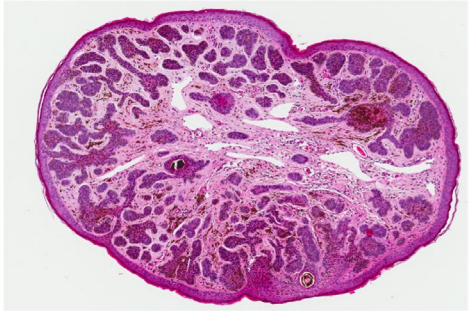

FIGURE 4

WHAT IS THE DIAGNOSIS?

Regula Wälchli and Nicole Knöpfel shared first authorship.

Diagnosis: **Nevoid basal cell carcinoma syndrome (NBCCS), also known as Gorlin syndrome**

Histopathological examination showed small nests and anastomosing strands of basaloid cells in the dermis partially connected to the epidermis with peripheral palisading and clefting from surrounding stroma, consistent with basal cell carcinoma. Pigment was found both within the tumor cells and in melanophages (Figure 4). Genetic testing for *PTCH1* was carried out and revealed the pathogenetic c.584G > A (p.(Arg195Lys) variant, which has been rarely described in NBCCS. The same mutation was detected in her mother, who also showed clinical characteristics of NBCCS. On clinical examination, numerous palmoplantar pits were found in our patient. Surveillance protocol for close monitoring of cutaneous and systemic manifestations of NBCCS was initiated.

DISCUSSION

NBCCS is a rare cancer-prone genetic disorder characterized by the development of multiple basal cell carcinomas (BCCs), odontogenic keratocysts of the jaw, palmar or plantar pits, calcification of the falx cerebri, and a high incidence of tumors, including childhood medulloblastoma, and ovarian and cardiac fibromas.[1] It is caused by germ line mutations in *PTCH1*, *PTCH2*, and *SUFU*, involved in Sonic Hedgehog signaling.[2] The disorder is inherited in an autosomal dominant fashion with almost complete penetrance and variable expressivity. Diagnosis of NBCCS is based on clinical criteria modified by Bree et al in 2013. Diagnosis may be delayed due to the late appearance of many cardinal features, with a reported mean age at diagnosis of 25 years. Thus, molecular testing is encouraged in patients with possible NBCCS not fulfilling clinical criteria, as well as in first-degree relatives of affected patients.

Proactive surveillance for systemic manifestations of GS including yearly brain MRI examinations to exclude medulloblastoma until age 8 years, avoidance of radiation, and emphasis on timely adoption of sun-protective measures is of utmost importance to reduce overall morbidity. Hence, pediatricians and dermatologists should recognize early clinical signs of NBCCS. At birth, infants may display macrocephaly. Additional early distinctive features include frontal bossing, coarse facies, hypertelorism, and facial milia around the eyes or on the forehead. Although periorbital milia have been reported to occur in 30% of patients, they are a poorly recognized early cutaneous feature of NBCCS.[3] In rare instances, affected individuals may develop cleft palate or cleft lip and eye abnormalities including congenital cataracts, orbital cysts, and microphthalmia.[3,4] Acral pits are commonly found in patients with NBCCS, but are not usually evident until later childhood. However, in our experience, palmoplantar pits can be present in infants and at preschool age as a pathognomonic feature, but are easily overlooked. BCCs are the hallmark of NBCCS and their clinical presentation is variable. Predilection sites of BCCs, which evolve from childhood onwards, are the face, neck, and trunk, including nonsun-exposed areas such as the axilla.[3] More recently, a striking phenotype of early onset of acral BCCs has been described in patients with GS.[5,6] BCCs in GS are nevoid lesions appearing as flesh-colored or pigmented papules, pedunculated lesions, nodules, or plaques. They may be mistaken for common nevi, molluscum, and skin tags or acrochordons.[7,8] The occurrence of these lesions in large numbers may also contribute to misdiagnosis. Indeed, our patient had a darker skin type and exhibited multiple pigmented BCCs that had been mistaken for melanocytic nevi. In such cases, dermoscopy may be a useful tool to achieve a correct diagnosis since no typical melanocytic structures are observed.[8]

Early nevoid BCCs in childhood usually do not behave aggressively, so a watchful waiting strategy and avoidance of invasive procedures is considered a reasonable approach.[5] Our patient's BCCs showed no evidence of invasive behavior over 4-year follow-up. Therefore, we opted for clinical follow-up and shave excision of the most aesthetically bothersome lesions on the face and trunk, with excellent result.

AUTHORS' CONTRIBUTION

Regula Wälchli and Nicole Knöpfel contributed equally and share first authorship.

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REFERENCES

1. Gorlin RJ. Nevoid basal cell carcinoma (Gorlin) syndrome. *Genet Med*. 2004;6(6):530-539.
2. Athar M, Li C, Kim AL, Spiegelman VS, Bickers DR. Sonic hedgehog signaling in basal cell nevus syndrome. *Cancer Res*. 2014;74(18):4967-4975.
3. John AM, Schwartz RA. Basal cell naevus syndrome: an update on genetics and treatment. *Br J Dermatol*. 2016;174(1):68-76.
4. Bree AF, Shah MR; BCNS Colloquium Group. Consensus statement from the first international colloquium on basal cell nevus syndrome (BCNS). *Am J Med Genet A*. 2011;155A(9):2091-2097.
5. Torrelo A, Vicente A, Navarro L, et al. Early-onset acral basal cell carcinomas in Gorlin syndrome. *Br J Dermatol*. 2014;171(5):1227-1229.
6. Coulombe C, Gagnon L-P, Larouche V, Dionne M-C. Infantile-onset palmo-plantar basal cell carcinomas and pits in Gorlin syndrome. *JAAD Case Rep*. 2018;4(7):662-664.
7. Pilkington S, McKinley LH, Miller RA. Pediatric nevoid basal cell carcinoma syndrome. *Cutis*. 2017;100(6):423-426.
8. Tiberio R, Valente G, Celasco M, et al. Pigmented basal cell carcinomas in Gorlin syndrome: two cases with different dermatoscopic patterns. *Clin Exp Dermatol*. 2011;36(6):617-620.